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THE SIGNIFICANCE OF VENOMS

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"A WEED," said Webster, "is a plant for which we have found no use." To be exact he should have added: "except in medicine"; for the oldest, and, until recently, the most empirical of the sciences has been the dumping ground for all products both plant and animal which had no other possible use.

In no case has this process been more persistent than with those products which have a marked physiological effect. It is to this persistent experimentation that we owe nearly all of the drugs of modern medicine. The venom of poisonous snakes has not been exempt, despite its great virulency. The facts that it retains its power when dried and powdered and that it is wonderfully uniform, and thus lends itself to a sort of standardization, have made it subject to no little exploitation. Had this exploitation been started twenty years earlier in the history of medicine, doubtless we should now have many records of "cures" resulting from its use. It came, however, at a time when the medical man had learned to be wary of new drugs, except those whose physiologic usefulness could be demonstrated.

Snake venoms from the other side of the therapeutic shield, that is, as agents to be combated rather than as medical ammunition, still hold interest to the point of fascination. In America this interest is disproportionate to the importance of its subject. In many regions all snakes, beneficial ones as well as venomous ones, have been exterminated, practically at least. It is true that along the southern Atlantic and Gulf coastal plains, the danger to man from the ever-present and vicious moccasin (*Ancistrodom piscivorus*) is a factor of some importance; and, in the southern part of the Rocky Mountain region, the western diamond-back rattler (*Crotalus atrox*) probably will not be exterminated for several decades. Elsewhere danger from snake bite is almost negligible.

Lest the statement in the last paragraph bring on my head a storm of protest, I shall mention a fact known to all naturalists; and that is that most snake bites are from non-venomous snakes. The colubers of the middle west are very belligerent serpents, and attack with satanic fury. Because of the hazel brown markings any member of this group is popularly branded as a "copperhead," a name which properly belongs to *Ancistrodon contortix,* a truly venomous reptile, but a small snake and

seldom or never found in plowed fields where the colubers go in their search for rodents. The region inhabited by the deadly moccasin is also frequented by enormous numbers of the red-bellied water snake (*Tropidonotus taxispilotus*) which is almost always called a "moccasin." The bite of this snake is harmless, aside from the actual mechanical injury, which may be considerable. Ditmars says of it: "It is in disposition one of the most ugly of American snakes." This is a mild statement. It is the experience of the writer that this water snake is the most depravedly vicious of all wild animals.

Do not these and other cases of errors in classification account for the success of some of the bizarre treatments which have been reported, some of them, to be frank, by even high-class medical men?

Venomous snakes have long been grouped according to the action of their venom. One extreme is represented by the rattlesnakes, whose venom is powerfully hemolytic, and acts on and through the circulatory system. The other extreme is represented by the cobras, asps, etc., whose venom acts much more rapidly and affects the nervous system directly. Noguchi refers to the two types of venom as "hemotoxic" and "neurotoxic."

Of more than passing interest is the fact that the tiny coral snake (*Elaps fulvius*) which is found in decaying logs and similar places in this country, carries a venom which is, as several workers have shown, qualitatively closely similar to that of the deadly cobra. But its sluggish and retiring disposition together with its small size make it inconsequential.

The moccasin and the copperhead, both members of the genus *Ancistrodon,* have a venom which seems to contain a little of the neurotoxic element, but its principal effect is much like that of the rattlesnakes.

There are, furthermore, a few small mildly poisonous snakes in America known to naturalists as Opisthoglyphs, because their fangs are grooved instead of tubular.

Despite the fact that the rattlesnakes contain two genera and a large number of species and vary greatly in color and general appearance, the natural history of American poisonous snakes is quite simple. The moccasin and the copperhead have exactly the same markings; but the former is very much darker in color, the pattern sometimes almost obscured.

Our *dangerous* snakes, then, may be said to be: First, those bearing a rattle; second, those having a series of dark brown hour-glass-shaped markings on a lighter brown background.

A further consideration to be borne in mind is that the venom of all of these is of the deoxidizing hemolytic type; and the standard potassium permanganate treatment has never been improved upon. The

Calmette anti-venomous serum widely advertised and sold by sporting-goods houses, while extremely useful against the effects of Oriental snakes, is useless in America. A limited quantity of anti-crotalus serum is put out by the Rockefeller Institution, but under experimental conditions this is said to be of rather doubtful value because of the large amount which must be used.

For some years the writer has carried on, intermittently, some investigations in connection with popular beliefs regarding the slightly venomous properties of certain snakes not generally considered poisonous by zoologists. The persistence of some of the rumors, and their confirmation in a few cases by medical men, gave him the idea that the presence or absence of the poison mechanism, grooved or tubular fangs and well-developed poison sac, may not always serve as a criterion of the reptile's potential venomousness. Unknown to the writer others, Alcock and Rogers, were carrying on similar investigations. No final results have yet been published; but the writer, at least, has been able in some cases not only to demonstrate the presence of a real toxic element, but actually to formulate quantitative terms.

Of course a snake which has not developed the proper poison mechanism for injecting its venom is not very dangerous, even if its saliva is quite toxic.

Weir Mitchell established many years ago a fact that had long been suspected: that the poison gland of a venomous snake is identical with the parotid salivary gland of mammals. Noguchi in his monumental work on snake venoms[1] has pointed out that this structure goes through quite an evolutionary series. To be brief: in the amphibia and certain reptiles, this gland is a pure mucous gland; and in the higher mammals it is a pure serous gland. In the poisonous snakes it is almost half mucous and half serous. The relatively high development as to size is undoubtedly a secondary adaptation to take advantage of the poisonous nature of the secretion.

The writer believes that in time it will be demonstrated that the transition, beginning with a simple recurved tooth, followed by the immobile grooved fang, and ending with the highly developed tubular and erectile fang, is also secondary and follows the development of the poison gland.

Furthermore, it would seem that the development of the neurotoxic element is also secondarily developed. Noguchi has shown that the division of snake venoms into hemotoxic and neurotoxic is a convenient, but arbitrary, arrangement. It seems that the fundamental substance is something of a hemolytic nature, always present, whose relatively slow action may be covered up by the neurotoxic element when the latter is present.

[1] Pub. 111, Carnegie Institution.

The old macroscopic distinction between serous glands and mucous glands is that serous glands are those whose membranous surfaces are closed to the outer air (the lining of the blood vessels, the pleura, and the peritoneum); mucous glands are those whose membranous surfaces are exposed at some point to the outer air (the lining of the alimentary canal, the lining of the genito-urinary machinery, etc.). Of course, there are important histological differences also. With this distinction in mind, the comparative anatomy of the parotid gland is more than suggestive of the mode of origin of the venom of snakes. The writer believes that the toxic quality is due to a surplus quantity of deoxidizing or correcting element.

Transitions occur in the venomousness of salivary secretions. Besides the cases referred to, Alcock and Rogers showed that the parotid secretion of *Zamenis mucosus*, one of the blacksnake tribe and usually considered a harmless snake, is distinctly toxic and a moderate dose is enough to kill small mammals. The writer has confirmed this in other species of *Zamenis* and certain other snakes. It is a rather striking fact, however, that the saliva of coluber and tropidonotus appears to be not in the least poisonous.

As to transition forms above the snakes, certain small mammals are at present under suspicion; particularly the small black skunk (*Mephitis mesomelas*), the alleged "hydrophobia skunk," often incorrectly called the civet cat.

It is more than likely that certain small mammals which, in various parts of the United States, are popularly thought to be "reservoirs" of hydrophobia, owe their reputation to a hemolytic element in their salivary secretions. The symptoms resulting from the bite of such an animal are exactly what an uninitiated person expects in hydrophobia. In fact the symptoms are much more in accord with the popular conception of hydrophobia than is genuine rabies itself. This is aside from the long period of incubation which rabies requires, and which is often overlooked.